

AMENDMENTS

A. IN THE SPECIFICATION:

Please insert the following replacement paragraphs:

B1 --[0072] For example, it is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid (*i.e.* isosteric and/or isoelectric mutations) will not have a major effect on the biological activity of the resulting molecule. Conservative replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids can be divided into four families:--

B2 --[0087] In addition to FasL fragments consisting only of naturally occurring amino acids, peptidomimetics or peptide analogues are also provided. Peptide analogues are commonly used in the pharmaceutical industry as non-peptide drugs with properties analogous to those of the template peptide. These types of non-peptide compounds are termed "peptide mimetics" or "peptidomimetics" (Luthman, et al., A Textbook of Drug Design and Development, 14:386-406, 2nd Ed., Harwood Academic Publishers (1996); Grante (1994) *Angew. Chem. Int. Ed. Engl.* 33:1699-1720; Fauchere (1986) *Adv. Drug Res.* 15:29; Veber and Freidinger (1985) *TINS*, p.392; and Evans, et al. (1987) *J. Med. Chem.* 30:1229, which are incorporated herein by reference). Peptide mimetics that are structurally similar to therapeutically useful peptides may be used to produce an equivalent or enhanced therapeutic or prophylactic effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (*i.e.*, a polypeptide that has a biological or pharmacological activity), such as naturally-occurring receptor-binding polypeptide, but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: -CH₂NH--, --CH₂S--, --CH₂CH₂--, --CH=CH-- (cis and trans), --COCH₂--, --CH(OH)CH₂--, and --CH₂SO--, by methods known in the art and further described in the following references:

B2 Spatola, A. F. in Chemistry and Biochemistry of Amino Acids, Peptides, and Proteins, B. Weinstein, eds., Marcel Dekker, New York, p. 267 (1983); Spatola, A. F., Vega Data (March 1983), Vol. 1, Issue 3, Peptide Backbone Modifications (general review); Morley (1980) *Trends Pharm. Sci.* pp. 463-468, (general review); Hudson, et al. (1979) *Int. J. Pept. Prot. Res.*, 14:177-185 (--CH₂NH--, CH₂CH₂--); Spatola, et al. (1986) *Life Sci.*, 38:1243-1249 (--CH₂--S); Hann (1982) *Chem. Soc. Perkin Trans. I*, 307-314 (--CH=CH--, cis and trans); Almquist, et al. (1980) *J. Med. Chem.*, 23:1392-1398, (--COCH₂--); Jennings-White, et al. (1982) *Tetrahedron Lett.* 23:2533, (--COCH₂--); Szelke, et al. (1982) European Appln. EP 45665 (--CH(OH)CH₂--); Holladay, et al. (1983) *Tetrahedron Lett.*, 24:4401-4404 (--C(OH)CH₂--); and Hruby (1982) *Life Sci.*, 31:189-199 (--CH₂--S--); each of which is incorporated herein by reference. One example of a non-peptide linkage is --CH₂NH--. Such peptide mimetics may have significant advantages over polypeptide embodiments, including, for example: more economical production, greater chemical stability, enhanced pharmacological properties (half-life, absorption, potency, efficacy, etc.), altered specificity (e.g., a broad-spectrum of biological activities), reduced antigenicity, and others.--

B3 --[0100] The FasL fragments, or derivatives thereof, and pharmaceutical compositions of the present invention are used in the treatment of or amelioration of inflammatory symptoms in any disease, condition or disorder where inflammation suppression would be beneficial. Inflammatory diseases, conditions or disorders in which the FasL fragments or derivatives thereof and pharmaceutical compositions of the present invention can be used to inhibit unwanted inflammation include, but are not limited to, optic neuritis; Devic's disease; encephalitis; myelitis; encephalomyelitis; acute disseminated encephalomyelitis; acute necrotizing hemorrhagic leukoencephalomyelitis; acute transverse myelitis; limbic encephalitis; post-polio syndrome; subacute sclerosing panencephalitis; Guillian-Barre syndrome; acute, subacute, and chronic neuropathy, in which there is radiculitis within the spinal canal; aseptic meningitis; chronic and recurrent meningitis; stroke; CNS trauma; CNS compression; infection;

B3 psychiatric diseases; inflammation or rejection after CNS transplantation; neurodegenerative diseases; Alzheimer's disease; Parkinson's disease; Huntington's disease; amyotrophic lateral sclerosis; HIV-related encephalopathy; and "stiff-man" syndrome.--

B4 --[0132] A summary of the clinical effects of rFasL treatment in acute EAE is shown in Table 1. Since the pain and stress might interfere with the EAE development in experimental animals (Kuroda Y. et al. (1994) *Brain Res Bull.* 34:15-17) due to the surgical procedures, the incidence of clinical EAE, the EAE onset, the peak EAE score and the loss of body weight during EAE between control-infused rats and non-infused rats were compared. These two groups did not differ significantly among any of the above four measures. This indicates that the procedure of intrathecal infusion as well as the ingredients in the control infusion solution did not interfere with the development of acute EAE. In rFasL treatment experiments, fifteen rats were each infused with 350 ng rFasL during 7~10 dpi. (MBP-immunized rats typically developed EAE on 10 dpi or 11 dpi.) It was found that clinical EAE was completely prevented in 12 rats (80%). In three other rats that developed EAE symptoms, the EAE onset was significantly delayed (12.3 ± 0.3 vs. 10.6 ± 0.2 , $p < 0.001$), and the EAE severity (0.8 ± 0.1 vs. 2.9 ± 0.2 , $p < 0.001$) and weight loss (22.3 ± 6.1 vs. 44.5 ± 2.1 , $p < 0.001$) were also significantly reduced.--

✓ Additionally, please insert the following replacement caption in Table 1, captions row, column 4:

--EAE onset (days past immunization)--